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## DEVELOPMENT OF A MODEL TO ASSESS ORTHOSTATIC RESPONSES

## Final Report

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## ABSTRACT

A major change for crewmembers during weightlessness in microgravity is the redistribution of body fluids from the legs into the abdomen, thorax, and head. The fluids continue to be sequestered in these areas throughout the flight. Upon reentry into gravity on landing, these same body fluids are displaced again to their normal locations, however, not without hazardous incidence to the crewmembers. The problem remains that upon landing, crewmembers are subject to orthostasis, that is, the blood flowing into the legs reduces the blood supply to the brain and may result in the crewmember fainting.

The purpose of this study was to develop a model of testing orthostatic responses of blood pressure regulating mechanisms of the cardiovascular system, when challenged, to maintain blood pressure to the brain. To accomplish this, subjects responses were assessed as they proceeded from the supine position to progressive head-up tilt positions of 30°, 60°, and 90° angles.

A convenience sample consisted of 21 subjects, females (N=11) and males (N=10), selected from a list of potential subjects available through the NASA subject screening office. The methodology included all non-invasive measurements of blood pressure, heart rate, echocardiograms, cardiac output, cardiac stroke volume, fluid shifts in the thorax, ventricular ejection and velocity times, and skin blood perfusion.

The Fischer statistical analysis was done of all data with the significance level at .05. Significant differences were demonstrated in many instances of change of posture for all variables. Based on the significance of the findings of this study, this model for assessing orthostatic responses does provide an adequate challenge to the blood pressure regulatory systems. While individuals may use different adaptations to incremental changes in gravity, the subjects, in aggregate, demonstrated significant adaptive cardiovascular changes to orthostatic challenges which were presented to them.

## INTRODUCTION

A major change for crewmembers during weightlessness in microgravity is the redistribution of body fluids from the legs into the abdomen, thorax, and head. The fluids continue to be sequestered in these areas throughout the flight. Upon reentry into gravity on landing, these same body fluids are displaced again to their normal locations, however, not without hazardous incidence to the crewmembers. Bungo (1989) observed that upon assuming an upright position on landing, orthostatic intolerance has been consistently observed after space flight. Greenleaf et al (1989) have recognized that physical exercise, pre-reentry fluid loading of the crew, and G-suit inflation have been used as countermeasures to maintain orthostatic tolerance. Melchior and Fortney (1993) described another countermeasure of lower body negative pressure (LBNP) applied during flight as another methodology to improve orthostatic tolerance of the crew upon landing of the orbiter. While there has been a modicum of success with these various protocols, none has successfully solved the problem of orthostatic intolerance of the crew. Since orthostasis can result in fainting, the safety of the crew and, especially, their ability to egress the orbiter in an emergency, becomes a priority. Refinement of these countermeasures previously described continues with ground based bedrest studies and in flight weightlessness studies.

The purpose of this study was to develop a model of testing orthostatic responses of the blood pressure regulating mechanisms of the cardiovascular system, when challenged, to maintain blood pressure to the brain. To accomplish this, subjects' responses were assessed as they proceeded from the supine position to progressive head-up tilt positions of 30°, 60°, and 90° angles.

## METHODOLOGY

The convenience sample consisted of 21 subjects, females (N=11) and males (N=10), selected from a list of potential subjects which was available at the NASA subject screening office. All subjects were required to have a current Air Force Class III physical examination and screening for drugs and HIV. The subjects were within the age range of 23-51 years (mean= 34 years), a range in height of 61-75 inches (mean=67 inches), and a range of weight of 107-211 pounds (mean= 147 pounds). The subjects were asked to abstain from alcohol ingestion for 48 hours prior to the tests and abstain from caffeine ingestion for 12 hours prior to the test. They were non-smokers and were not taking any prescription drugs.

Upon arrival at the laboratory, the subject changed into shorts, a t-shirt and athletic shoes. Weight and height were measured and recorded. The investigator then requested the subject to lie in a supine position on a circoelectric bed for a period of 30 minutes to establish baseline data at 0°. At 25 minutes of the rest period, data was collected for 5 minutes. At the end of this period, the bed was tilted to a 30° angle for 5 minutes, and successively to 60° and 90° angle (standing position) tilts, each for 5 minutes. The angles correspond to gravity increments (obtained from the sines of the angles) from +0.50 g (30°), +0.87 g (60°), to +1 g (90°). The time to change from one position to another was an average of 6 seconds. The subject was then returned to

the supine position at 0° for five minutes for recovery. Data was collected continuously which included blood pressure (manually), heart rate, electrocardiogram, echocardiogram, fluid shifts within the thorax, and laser doppler measurement of skin blood perfusion of the left forearm and calf of the left leg. All measurements were non-invasive. Each subject spent approximately one hour in testing. The ambient temperature of the laboratory was an average 22° C. This investigator explained the protocol to each subject and informed consent was obtained before the subject's participation.

Blood perfusion and blood flow velocity of the skin of the inner aspect of the left forearm and outer aspect of the left calf of the leg were measured by placing a surface laser probe in both locations. To avoid vasoconstriction from a cool environment, the probes were placed in circular heaters which surrounded the probe with an opening at the bottom for access of the laser to the skin. The heaters were fixed to the skin with adhesive disks. The temperature of the heaters was 38° C. Data was collected continuously on a Perimed Laser Doppler Instrument and recorded simultaneously on a computer with a visual graphic display of the data.

Fischer et al (1986) described laser doppler flowmetry as a method of measurement of red blood cell flux within the capillary bed. As light reflects a moving object, it changes its frequency in proportion to the velocity of the moving object. The light is transmitted to the skin surface through a fiberoptic cable and reflected back through the cable to the instrument for analysis.

Cardiac stroke volume was measured by continuous wave Doppler method. Data was collected through skin electrodes placed on the subject's thorax. The pulse velocity was measured at the suprasternal notch where aortic diameter was measured by m-mode echocardiography. Cardiac output was calculated by multiplying the cardiac stroke volume by the heart rate.

The Biomed Instrument was used to measure thoracic impedance or fluid shifts in the thorax. Two skin electrodes were placed on the subject on either side of the neck and two on the lower chest.

Blood pressure measurements were made manually each minute during the baseline, 5 minute intervals, and at the end of recovery. An aneroid sphygmomanometer and stethoscope were used for collecting this data.

A Finapres instrument was attached to the subject's left middle finger with an inflated cuff. This instrument was used to observe graphically displayed blood pressure trends and digital readout of blood pressure, heart rate, and pulse pressure.

## RESULTS

Statistical analyses were done using the Fisher test for significant difference at the .05 level for all variables. For this report, data are presented for 13 subjects because the data analyses is not yet completed for the remaining 8 subjects.

## HEART RATE

The mean heart rate ranged from 59 to 75 beats per minute; the stroke volume ranged from 51 to 88 beats per minute; and the cardiac output ranged from 3757 to 5360 ml/minute over the entire testing period.

Mean heart rate was at its minimum at the end of the 5 minute recovery period when the subject was returned to the supine position, which was slightly lower than the mean of the baseline rest period at the beginning of the test. The heart rate increased progressively to its maximum at 90° head-up tilt.

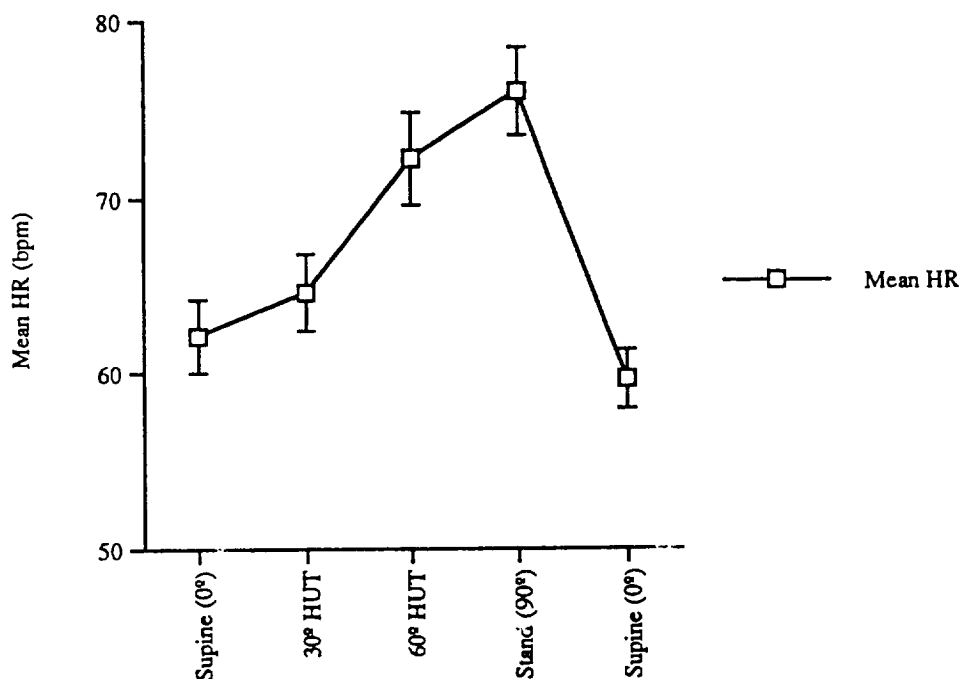


Figure 1. Mean Heart Rate (HR) Responses For All Positions

## STROKE VOLUME

The stroke volume reached its maximum level at the end of recovery when the subject was returned to the supine position. This was slightly increased over the baseline mean. The stroke volume progressively decreased at 30°, 60°, and reached a minimum at 90° headup tilt.

## CARDIAC OUTPUT

The mean cardiac output reached its highest level during recovery with the subject in supine position at the end of the test. It was slightly higher than at baseline. The cardiac output decreased progressively from the baseline to the 90° headup tilt position when it reached its lowest value.

The cardiac output was significantly different from the supine baseline position to 30°, 60°, and 90° head-up tilt positions; from 30° head-up tilt position to 90° head-up tilt and supine position of recovery; from 60° and 90° head-up tilt positions to the supine position of recovery.

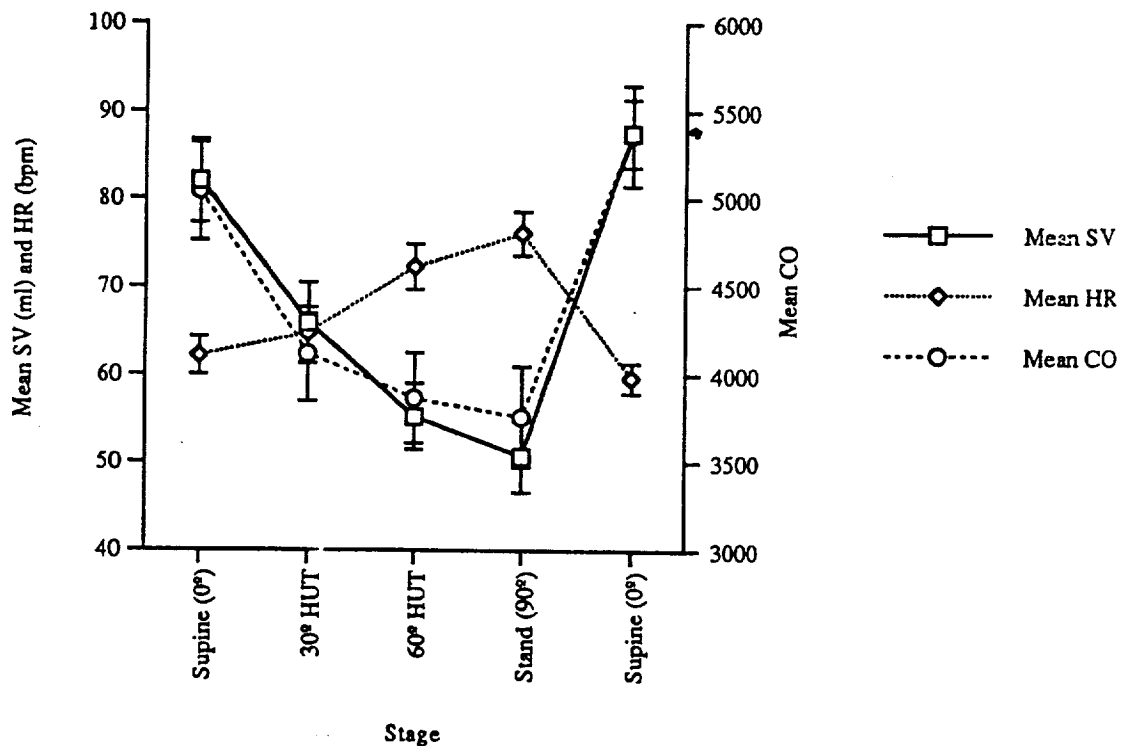


Figure 2. Mean Heart Rate(HR), Stroke Volume(SV) and Cardiac Output(CO) For All Positions

The supine heart rate was significantly different from the 30°, 60°, 90° and supine recovery positions; different from the 30° position to the 60°, 90° head-up tilt and supine recovery position; between 60° and 90° head-up tilt position and supine recovery position; and between 90° head-up tilt position and supine recovery position.

### VENTRICULAR EJECTION TIME AND EJECTION VELOCITY INDEX

The mean ventricular ejection time (VET) had only slight variation during the test with the exception of the supine position of recovery at the end of the test. The mean ejection velocity index (EVI) progressively decreased from the supine baseline position to the 60° head-up tilt position. It remained essentially the same for the 90° head-up tilt position and then increased with the supine position during recovery at the end of the test.

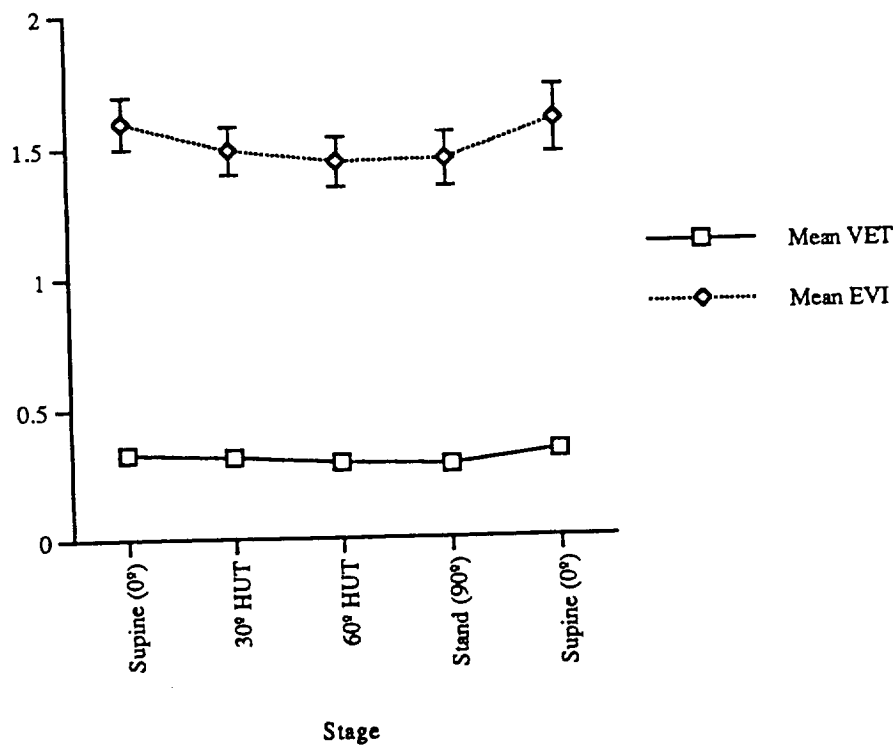


Figure 3. Mean Ventricular Ejection Time(VET) and Ejection Velocity(EVI) For All Positions

The VET was significant at the .05 level at all points: baseline supine compared with 30°, 60° and 90° head-up tilt, supine recovery position; 30° head-up tilt compared with 60°, 90° head-up tilt and supine position of recovery; between 60° and 90° head-up tilt and supine recovery position; and between 90° head-up tilt and supine recovery position. The EVI had significant differences between the supine baseline position and 60° and 90° head-up tilt positions; between 30° head-up tilt and supine recovery position; between 60° and 90° head-up tilt and supine recovery position.

The supine baseline stroke volume was significantly different from the 30°, 60° and 90° head-up tilt positions and supine recovery position; and from the 30° position to the 60°, 90° head-up tilt positions and supine recovery positions; and between 60° and 90° head-up tilt positions to the supine recovery position.

### SYSTOLIC BLOOD PRESSURE

The systolic blood pressure had small incremental increases from the baseline supine position until the 90° head up tilt position when there was a slight decrease. The mean increased during the supine recovery period at the end of the test, above the baseline value. Systolic blood pressure was not significant at the .05 level in any of the comparisons of positions.

### DIASTOLIC BLOOD PRESSURE

The diastolic blood pressure increased from the supine baseline position to the 60° head-up tilt position, decreased slightly at the 90° head-up tilt position and then decreased during the supine position for recovery at the end of the test.

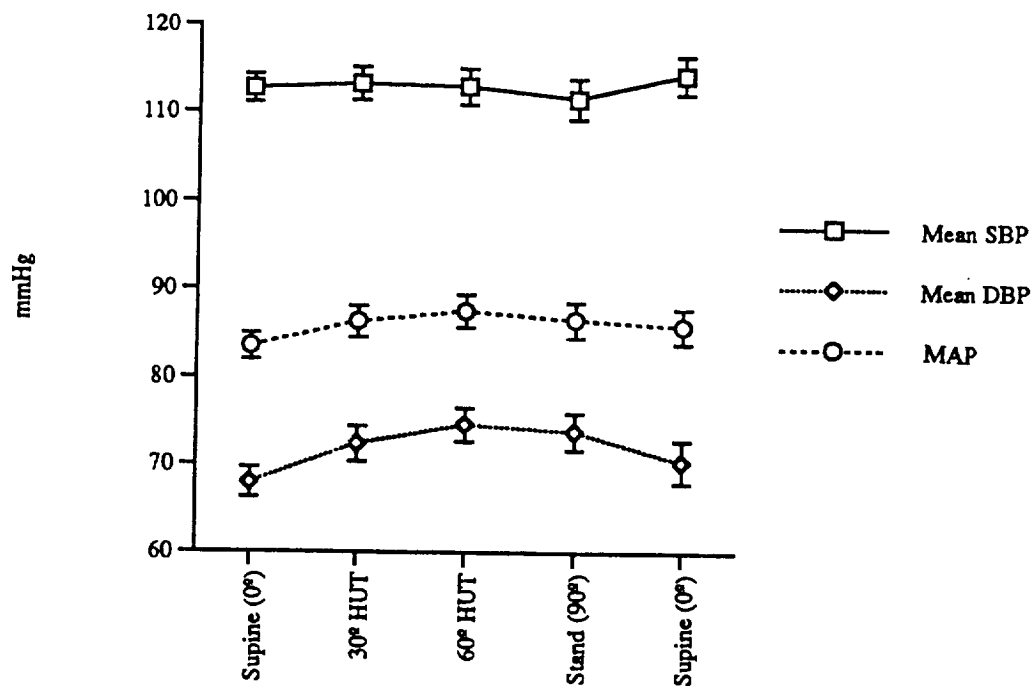


Figure 4. Mean Systolic(SBP), Diastolic Blood Pressure(DBP) and Mean Arterial Pressure(MAP) For All Positions.

The diastolic blood pressure significantly differed from the baseline supine position to the 30° head-up tilt; from supine to 60° head-up tilt position; from the supine to the 90° head-up tilt; and between 30° head-up and tilt 60° head-up tilt and supine recovery position; between 60° and 90° head-up tilt and supine recovery position.



## ARTERIAL PRESSURE

The mean arterial pressure follows the diastolic blood pressure response with at greater difference at the supine recovery position.

The mean arterial pressure was significantly different from the supine baseline position to the 30° head-up tilt; from the supine to the 60° and 90° head-up tilt positions; between the 60° and 90° head-up tilt positions and supine position during recovery.

## PULSE PRESSURE

The mean pulse pressure progressively decreased from the supine resting position to its minimum value at 90° head-up tilt. Its maximum value was at the supine position during recovery, but only slightly more than baseline resting.

Significance of the pulse pressure differences were from the supine baseline position to 30°, 60°, and 90° head-up tilt positions; between 30°, 60° and 90° head-up tilt positions to supine position during recovery.

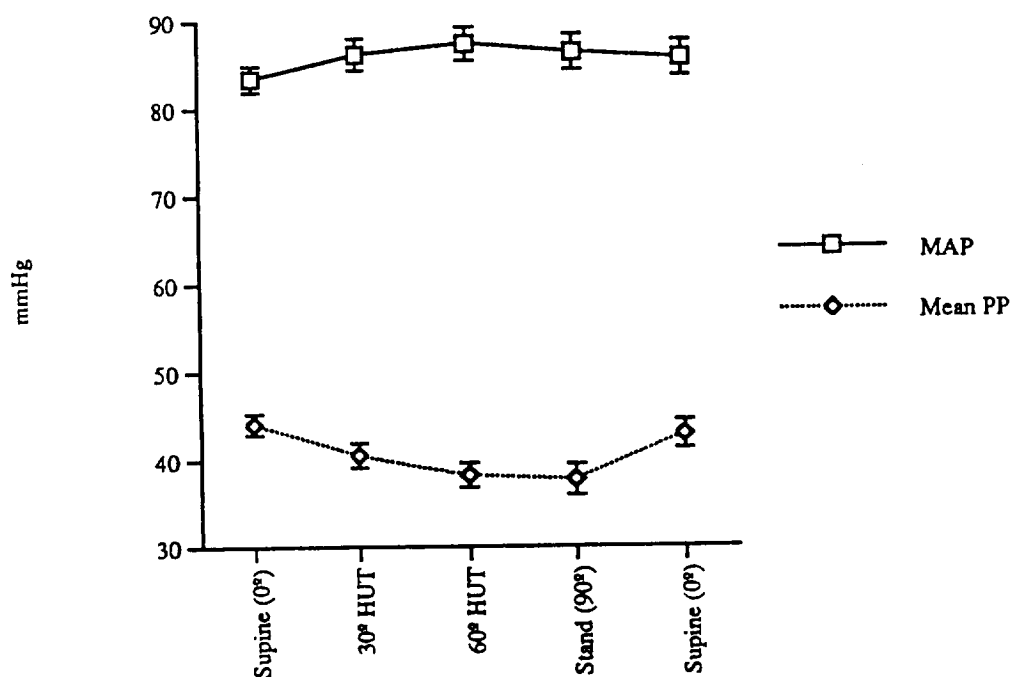


Figure 5. Mean Arterial Pressure(MAP) and Pulse Pressure(MPP)  
For All Positions

## THORACIC FLUID INDEX

The Thoracic Fluid Index (TFI) increased in a steep slope from the supine resting position to 90° head-up tilt where it plummeted during the supine position recovery phase to a value slightly lower than supine baseline.

Significance of the TFI across tilt positions occurs at the .05 level for all comparisons except when supine resting was compared to supine recovery. As the values decrease, the fluid shifting increases.

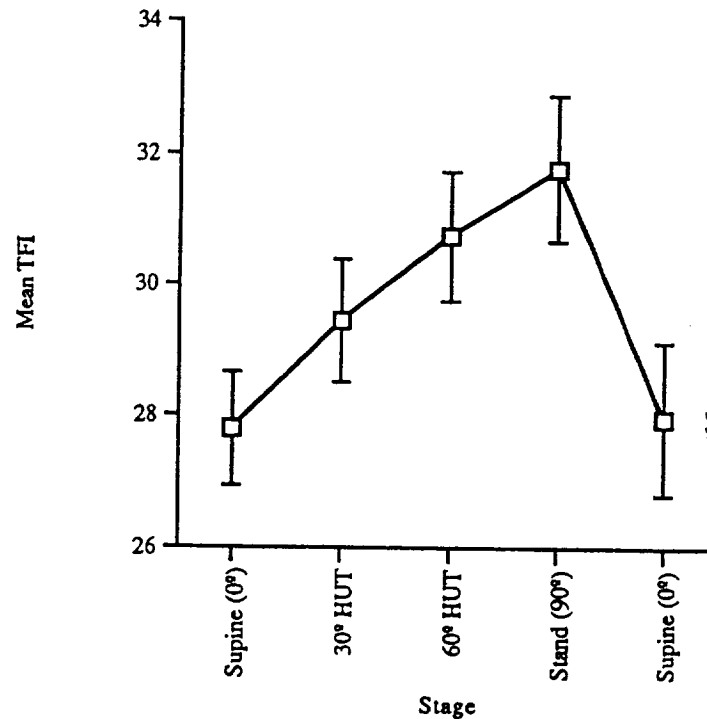


Figure 6. Mean Thoracic Fluid(TFI) Index Response For All Positions

#### SKIN BLOOD PERFUSION

Laser doppler monitoring of blood perfusion of the skin is reported for velocity, volume, and combined mass of blood cells taken from blood flow of the left forearm and the lateral side of the calf of the left leg. Within the skin of the arm, the mean velocity was at minimum values at the supine baseline and at the 90° head-up tilt position. During the supine position during recovery, the blood velocity values are at its maximum. The blood volume increased slightly from the supine baseline to the 90° head-up tilt and then decreased slightly during the supine position of recovery. The combined mass of blood cells followed this same pattern as would be expected.

There was significant change in blood velocity in the skin of the arm when supine baseline position and the 90 head-up tilt position were compared to the supine recovery position. The combined mass of blood cells was significant when the supine baseline was compared with the 90 head-up tilt position; when 30 head-up tilt was compared with the 90 head-up tilt; when 30 head-up tilt was compared with supine position during recovery; and when 60 head-up tilt position was compared to 90 head-up tilt position. The blood volume was significantly different when the supine baseline was compared with 90 head-up tilt position and the supine position during recovery; 30 head-up tilt was significantly different from 90 head-up tilt and supine position during recovery; and 60 head-up tilt was significantly different from the supine position during recovery.

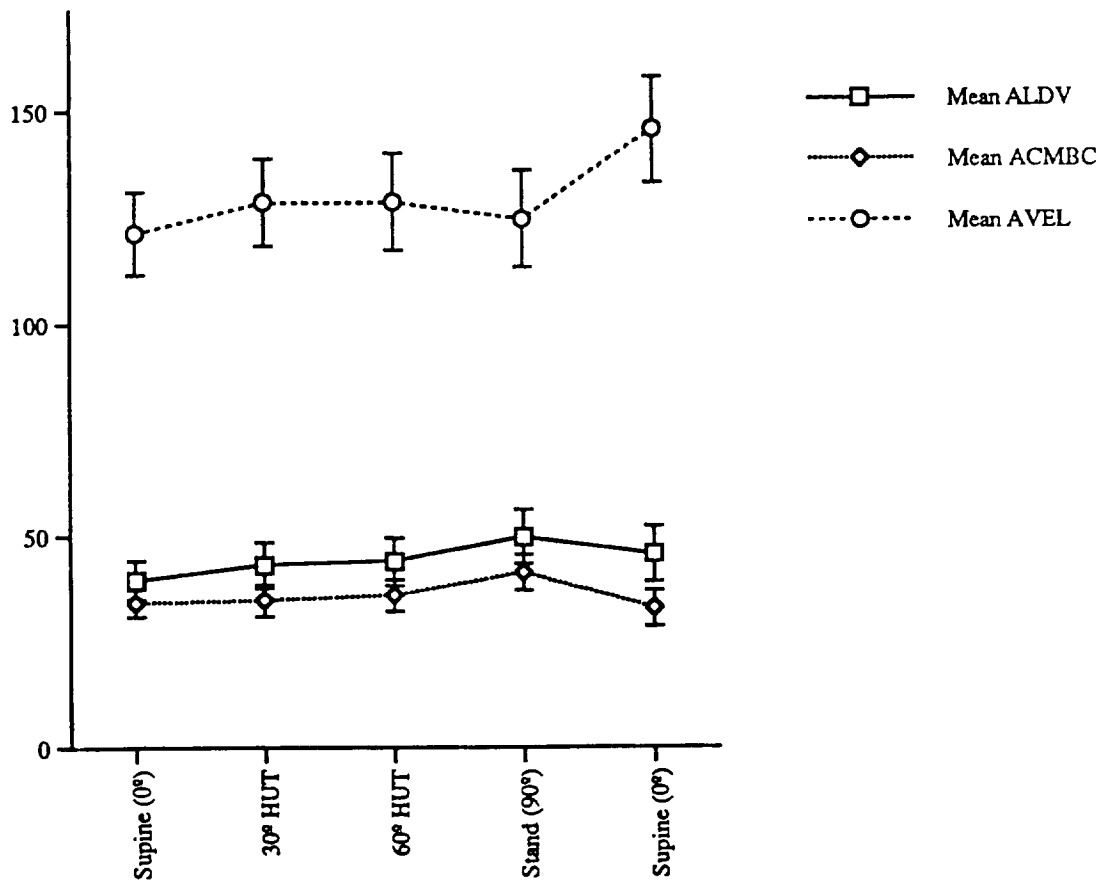


Figure 7. Mean Blood Velocity(AVEL), Volume(ALDV), and Combined Mass of Blood Cells(ACMBC) Of The Skin Of The Arm

The blood velocity of the skin of the left leg decreased progressively from the supine baseline position to 90 head-up tilt and then sharply increased during the supine position of recovery at the end of the test. The blood volume and combined mass of blood cells followed this same pattern.

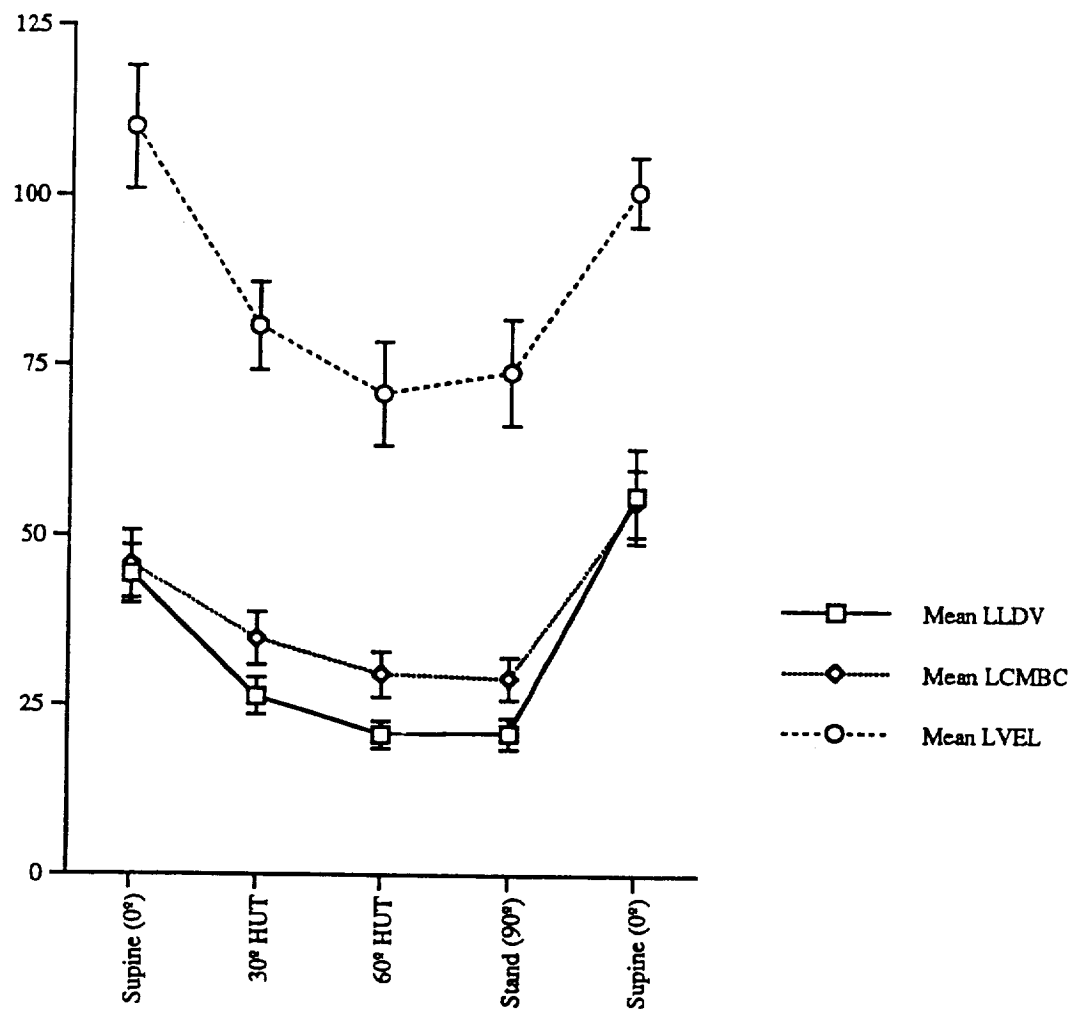


Figure 8. Mean Blood Velocity(LVEL), Volume(LLDV), and Combined Mass of Blood Cells(LCMBC) Of The Skin Of The Leg For All Positions

There were significant differences in velocity between supine baseline and 30° head-up tilt, 60° head-up tilt, and 90° head-up tilt; between 30°, 60°, and 90° head-up tilt and supine position of recovery. There were significant differences in volume from the supine baseline position and the 30° head-up tilt, 60° head-up tilt, and 90° head-up tilt; between 30° head-up tilt and supine position of recovery; and between 60° and 90° head-up tilt positions and supine position of recovery.

The areas of significance for combined mass of blood cells was from the supine baseline position to 30°, 60° and 90° head-up tilt positions. There were significant differences between the 30° head-up tilt and 60° and 90° head-up tilt and supine recovery position. The head-up tilt positions of 30°, 60°, and 90° all differed from the supine position of recovery.

## DISCUSSION

Most subjects tolerated the tests very well. Only one subject indicated that a

feeling of lightheadedness or dizziness accompanied the changes in posture from supine to the three different angles. However, each of the subjects perceived the supine recovery position as a head-down tilt when it was actually at zero position. Subjects were asked not to actively stand on the foot board at 90° but to remain as passive as possible to avoid activating skeletal muscles which would influence blood flow in the legs. Two restraining fabric bands across the body, one above the knees and the other just below the waist, helped the subjects to maintain as passive a position as possible. Even though, the subjects were in a 90° position, some perceived that their bodies were tilted beyond this angle.

All subjects showed an immediate and incrementally increasing heart rate when their posture was changed to the three head-up tilt positions. Total peripheral resistance followed this same pattern. This was accompanied by decreasing stroke volume and cardiac output. While systolic blood pressure had only slight variations until it decreased at the 90° head-up tilt, diastolic blood pressure increased incrementally with the angle changes and then also decreased at 90° head-up tilt. The mean arterial pressure followed this same response. Pulse pressure incrementally decreased with the lowest point at 90° head-up tilt. Ventricular ejection time and ejection velocity decreased only slightly from supine to 90° head-up tilt.

Mekjaviv et al (1987) induced significant ( $P = .005$ ) increases in diastolic pressure, but no significant differences in systolic pressure when taking subjects from a supine position to a 70° head-up tilt. They made the assumption that the upright posture elevated the heart rate. Ten Harkel et al (1992) postulated that increases in diastolic and mean blood pressure and heart rate following a change in posture from 6° head-down tilt to standing reflected a redistribution of blood volume followed by vasoconstriction, a decrease in stroke volume and cardiac output.

Skin blood perfusion, measured with laser doppler, of the arm and leg differ. The velocity of blood flow of the skin of the arm increased until 90° head-up tilt, then slightly decreased. Blood volume of the skin of the arm increased to 30° head-up tilt, stabilized at 60° and dropped at 90° head-up tilt. These responses reflect the activity of the baroreceptors as they cause a reflex vasoconstriction to maintain blood pressure during the standing position. The velocity of blood perfusion in the skin of the leg decreased to 60° head-up tilt, then increased at 90° head-up tilt. Blood volume in the skin of the leg decreased until 60° head-up tilt, then increased at 90° head-up tilt. The decrease in blood velocity and volume in the skin of the leg probably reflects the shift of body fluids to the chest and then at the 90° head-up tilt or standing, the blood responds to the gravitational pull and increases in velocity and volume.

Johnson (1986) demonstrated that skin blood flow is determined by more than thermoregulation and that baroreceptor reflexes have a major function in cutaneous circulation. When blood pressure regulation is challenged, cutaneous vasoconstriction occurs in normothermic subjects.

Blomquist et al (1983) estimated that changing posture from supine to an upright position increases the venous volume of the legs by approximately 650 ml. with an

additional volume of 250 ml. of blood transferred to the veins in the buttocks and the pelvic veins.

Most of the previous studies(Sander-Jensen et al, 1986; Mekjavic and Mittleman, 1987; and Ten Harkel et al, 1992) that have compared either the supine position or a head-down position ranging from  $-6^{\circ}$  to  $-10^{\circ}$  with responses of subjects at various head-up tilt positions have had similar responses as demonstrated in this study. However, there were differences of methodology. In most other studies, rest periods were of longer duration at the beginning of the test and between the increasing of the angles of head-up tilt. Others took the subject from the supine position immediately to a  $70^{\circ}$  head-up tilt. In this study, with a relatively short rest period of 30 minutes for baseline, significant cardiovascular changes occurred immediately upon changing posture to each increment of  $30^{\circ}$ ,  $60^{\circ}$  and  $90^{\circ}$  head-up tilts within a 5 minute period of each other. While the subject was not retained in a particular position until stabilization, the responses continued to change with each angle or change in gravitational force acting upon the body. Without exception, when the subjects were returned to the supine position during recovery, all variables responded in the direction of baseline values and in some cases overshooting the baseline. Data collection was limited to a 5 minute recovery period, actual recovery may have extended beyond that time.

## CONCLUSION

Based on the significance of the findings of this study, this model for assessing orthostatic responses does provide an adequate challenge to the blood pressure regulatory systems. While individual subjects may use different adaptations to incremental changes in gravity, such as increased heart rate, increased peripheral resistance, increased diastolic blood pressure or increased stroke volume; in the aggregate, the subjects demonstrated significant adaptive cardiovascular changes to orthostatic challenges which were presented to them.

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